REMARKS

In the Final Action dated December 2, 2003, Claims 30-36 are pending and are under consideration. Claims 30-36 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enabling support. In a Response dated June 2, 2004 to the Final Action, Applicants amended Claim 30 and canceled Claim 32, without prejudice. In the Advisory Action dated August 4, 2004, the Examiner stated that Applicants' Amendment filed on June 2, 2004, was not entered, allegedly because the Amendment raised new issues that would require further consideration and/or search.

This Response addresses the Examiner's rejection in the Final Action. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 30-36 are rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Claims 30-36 are drawn to a method of inhibiting the proliferation of malignant breast cancer cells in a mammal by administering a selected cytokine, e.g., oncostatin M (OSM). The Examiner alleges that it would require undue experimentation for one skilled in the art to make and use the invention. The Examiner specifically alleges that Applicants have provided little or no guidance relating to methods of inhibiting the proliferation of malignant breast cancer cells in mammals comprising administering OSM.

In response, Applicants respectfully submit that Claims 30-36 are fully supported by the instant disclosure. The Examiner acknowledges on page 4 of the Final Action that a considerable amount of time of experimentation is permissible if the skilled artisan is given sufficient direction or guidance. Applicants respectfully submit that such direction and guidance are provided throughout the specification.

Applicants observe that the specification on page 14, lines 5-15 discloses the amount of cytokine that can be administered to a mammal as well as the frequency of administration. Page 15, lines 6-14 of the specification discloses, as an example, an effective amount of a cytokine that can be administered to a mammal to treat breast cancer as well as the frequency of

administration. Page 14, lines 17-26; page 15, lines 3-6; page 17, lines 27-30; and page 18, lines 1-4 of the specification disclose suitable modes of administering cytokines. Applicants further observe that the specification on page 15, lines 7-30 and page 16, lines 1-30 discloses pharmaceutical forms suitable for administration, e.g., for injection or oral administration.

The Examiner also alleges that the basis for his rejection was previously set forth on pages 5-9 of the February 21, 2003 Official Action. In the February 21, 2003 Official Action, the Examiner alleged that the specification does not provide any guidance or exemplification of any correlation between inhibiting proliferation of a breast cancer cell line in the presence of OSM *in vitro* and administering OSM to a mammal to inhibit the proliferation of malignant breast cancer cells *in vivo*. The Examiner has also cited a number of references which discuss various obstacles in cancer therapy. The Examiner concludes that one skilled in the art would be forced into undue experimentation to practice the claimed invention.

Applicants respectfully submit that the present application recognizes for the first time that cytokines, such as oncostatin M (OSM), interleukin-6 (IL-6), interleukin-11 (IL-11), leukemia inhibitory factor (LIF) and epidermal growth factor (EGF), have inhibitory effects on the proliferation of malignant breast cancer cells. The specification provides a thorough characterization of the inhibitory effects of OSM on the proliferation of malignant breast cancer cells *in vitro*, including the inhibitory doses, and the effects on cell cycle, cell morphology and the expression of various cell surface receptors. See pages 31-38 of the specification, for example. In addition, the specification provides exemplification of the inhibitory effects on the proliferation of malignant breast cancer cells *in vitro* of other cytokines, including EGF (e.g., at pages 32 and 34), IL-6 (e.g., pages 36-37), LIF (e.g., pages 36-37) and IL-11 (e.g., pages 36-37).

Applicants respectfully submit that those skilled in the art would consider that the *in vitro* characterizations provided in the specification are reasonably correlated to inhibitory effects of the selected cytokines on the proliferation of malignant breast cancer cells *in vivo*. Applicants do not dispute that obstacles may exist, or that additional experimentation may be required to optimize the parameters for *in vivo* administration of a selected cytokine. However,

there is no evidence that the obstacles constitute undue experimentation. Moreover, some experimentation is permissible. *In re Wands*, 858 F.2d 731, 736-737, 8 U.S.P.Q. 1400, 1404 (Fed Cir. 1988). Necessary experimentation is not determinative of the question of enablement; only undue experimentation is fatal under the provisions of 35 U.S.C. §112, first paragraph. *Id* (emphasis added). The specification, as outlined above, provides sufficient direction and guidance to those skilled in the art to practice the claimed methods of inhibiting the proliferation of malignant breast cancer cells in mammals comprising administering a cytokine. Applicants respectfully submit that based on the teaching provided in the specification, those skilled in the art would be able to practice the claimed methods without undue experimentation.

Therefore, it is respectfully submitted that the rejection under 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of the rejection is respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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